Remarks

Reconsideration and withdrawal of the rejections set forth in the Office action dated September 14, 2005 are respectfully requested. Applicants petition the Commissioner for a 1-month extension of time. A separate petition accompanies this amendment.

I. Amendments

A. In the Specification

The specification is amended to identify sequences with sequence identifiers in accord with 37 C.F.R. § 1.821(d).

B. In the Claims

Claims 23 and 30 are canceled.

Claims 1 and 27 are amended to recite wherein the agent comprises a transduction agent in the p75 signal transduction pathway or a variant or fragment thereof, or an agent capable of specifically interacting with the transduction agent in the p75 signal transduction pathway; and wherein the agent is bound to a PTD domain. Basis for these amendments can be found in original claims 23 and 30.

Claims 21 and 27 are further amended to recite a composition for regenerating nerves.

Claim 27 is additionally re-written in independent form.

Claims 25-26 and 29 are amended to remove matter allegedly directed to non-elected species.

Claim 29 is amended to recite the SEQ ID NO for Pep5.

No new matter is added by way of these amendments.

II. Sequence Compliance

The specification was objected to for disclosing an amino acid sequence which is not identified by a sequence identifier. Applicants have amended the

specification in accord with 37 C.F.R. 1.821(d). Accordingly, Applicants respectfully request withdrawal of the objection to the specification.

III. Objections to the Claims

Claims 25, 26, and 29 were objected to for alleged informalities. Specifically, the claims recite multiple non-elected species. Although Applicants do not necessarily agree with the Examiner's assertion regarding the non-elected species, the claims are amended to expedite prosecution. It is Applicants' belief that claims 25, 26, and 29, as amended, read on the elected species. Accordingly, Applicants respectfully request withdrawal of the objections to the claims.

Claims 27 and 28 were objected to under 37 C.F.R. § 1.75(c) as being in improper dependent form. The claims are amended in accord with the Examiner's kind suggestion.

IV. Priority

Applicants enclose herewith a certified copy of the Japanese priority application. Applicants submit they have now complied with all of the requirements of 35 U.S.C. § 119(a)-(d) for foreign priority.

V. Rejection under 35 U.S.C. §112, first paragraph

Claims 21-23 and 25-30 were rejected under 35 U.S.C. §112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claims 21-23 and 25-30 were further rejected under 35 U.S.C. §112, first paragraph, allegedly because the specification does not enable any person skilled in the art to which it pertains, or with which it is most connected to make and use the invention commensurate in scope with the claims.

These rejections are respectfully traversed.

A. Written Description

Claims 21 and 27, as amended, clarify the agents are capable of inhibiting a p75 signal transduction pathway, wherein the agent comprises a transduction agent in the p75 signal pathway or an agent capable of specifically interacting with the transduction agent in the p75 signal transduction pathway. The specification discloses at least 11 transduction agents (see paragraph [0515]) and at least 6 agents capable of specifically interacting with a biological agent (see paragraph [0513]). The term "agent capable of specifically interacting with" is defined in paragraph [0513] as "an agent which has an affinity to the biological agent." Thus, it would be clear to one skilled in the art that "an agent capable of specifically interacting with the transduction agent in the p75 signal transduction pathway" refers to an agent that specifically binds to the transduction agent. As also described in paragraph [0513], this affinity can be measured with methods well known in the art such as hybridization assays and a binding assays. By way of example, the Examiner is specifically directed to Examples 2-4, on pages 341-369, which specifically disclose a number of different compounds that were used to regenerate nerves. As such, the Applicants have sufficiently described the genera of agents claimed.

The Examiner next asserts that the definition of the Pep5 protein is not a limiting definition of Pep5 as the specification includes all variants and fragments of Pep5, provided that the fragments have biological activity.

With regard to Pep5 fragments, the fragments of the agent Pep5 are specifically defined (see paragraph [0472]). One skilled in the art would readily be able to determine the motifs of proteins that are important for activity and would recognize probable fragments that would retain activity. Furthermore, the biological activity of an agent for use in the claimed method can be easily confirmed by measurement with a Rho activity assay which blocks activation of Rho

by a myelin-derived protein as described in paragraph [0472]. Therefore, one skilled in the art would be easily able to make and use variants and fragments of Pep5 encompassed by the recitations of the claims.

Accordingly, Applicants submit that these teachings in the specification show that Applicants were in possession of the invention as presently claimed at the time of filing.

B. Enablement

The first paragraph of 35 U.S.C. §112 requires that the specification of a patent enable any person skilled in the art to which it pertains to make and use the claimed invention without undue experimentation (e.g., *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir., 1991).

The enablement requirement is met if the description enables any mode of making and using the claimed invention (*Engel Industries, Inc. v. Lockformer Co.*, 946 F.2d 1528, 20 USPQ2d 1300 (Fed. Cir. 1991).

The Examiner acknowledges that the specification is enabling for certain agents, but asserts that the entire scope of the claims is not enabled, as a structural limitation is not recited. Therefore, the Examiner concludes that one skilled in the art would require undue experimentation to make and use compositions commiserate with the scope of the claims.

As noted above, the specification discloses at least 11 specific transduction agents and at least 6 agents capable of specifically interacting with a biological agent. Further, methods of screening agents for activity are well known in the art. As such, the claimed invention is well within the scope of expected experimentation for one skilled in the art.

The Examiner further asserts that the specification does not include working examples to support the broad definitions of "variant" and "fragment," as the activity of fragments of proteins involved in the p75 pathway cannot always be predicted.

Furthermore, the Examiner asserts that the specification provides no guidance to the artisan in the selection of which variants will work in the method.

The Mukai reference cited by the Examiner to demonstrate different activity of different fragments of the same peptide actually counteracts the statement that one skilled in the art would have no guidance as to which variants would work in the claimed method. Specifically, Mukai teaches that one skilled in the art would realize that motifs of proteins are important for activity, and would likely not choose to use a "fragment" consisting of a single amino acid. From the teaching in the Mukai reference, it is clear that one skilled in the art would recognize probable fragments that would retain activity.

The Examiner also asserts that the p75 signal transduction pathway is complex, and states that there is no structural limitation on the transduction agents or on agents capable of interaction with the structural agents. As such, the Examiner asserts that one skilled in the art would have to undertake undue experimentation to make and use the claimed compositions.

The specification describes methods enabling one skilled in the art to easily screen and identify the transduction agents. The Examiner is directed to paragraphs [1199] to [1202], which describe a typical manner in which an agent functions to inhibit the p75 pathway. Therefore, the combination of the teaching in the specification and the knowledge of one skilled in the art are sufficient to allow one skilled in the art to obtain a desired agent without undergoing undue experimentation. Further, as the p75 signal transduction pathway is known to be complex, a certain amount of experimentation would be expected by one skilled in the art. This experimentation is standard in the art using standard techniques.

Therefore, the combination of the teaching in the specification and the knowledge of those skilled in the art enable those skilled in the art to make and use the claimed invention without undue experimentation.

In light of the teaching in the specification and Applicant's amendments, Applicants submit that the present claims satisfy the requirements of §112, first paragraph and respectfully request that the rejections be withdrawn.

VI. Rejection under 35 U.S.C. § 112, second paragraph

Claims 28-29 were rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

The Examiner first objected to the language "wherein the nerve" in claim 28 as lacking antecedent basis. Claim 28, as amended, provides proper antecedent basis for the objected language.

Second, the Examiner objected to the language "a Pep5 polypeptide" in claim 29 as allegedly not being defined in a limiting fashion. Claim 29, as amended, specifically recites the sequence identifier for the Pep5 polypeptide.

In view of the above, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 112, second paragraph.

VII. Rejection under 35 C.F.R. § 102

Claims 21-23 and 25-29 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Ilag *et al.* (*Biochemical and Biophysical Research Communications*, 255:104-109, 1999).

These rejections are respectfully traversed.

A. The Present Invention

The presently claimed invention relates to a composition for regenerating nerves, comprising an agent capable of inhibiting a p75 signal transduction pathway, wherein the agent comprises a transduction agent in the p75 signal transduction pathway or a variant or fragment thereof, or an agent capable of specifically interacting with the transduction agent in the p75 signal transduction pathway; and wherein the agent is bound to a PTD domain (claim 21) and a

composition for regenerating nerves comprising an agent capable of inhibiting a p75 signal transduction pathway, wherein the agent comprises a transduction agent in the p75 signal transduction pathway or a variant or fragment thereof, or an agent capable of specifically interacting with the transduction agent in the p75 signal transduction pathway, wherein the composition is suitable for *in vivo* or *in vitro* administration forms (claim 27).

B. The Prior Art

ILAG ET AL. describe selection of a peptide ligand to the p75 neurotrophin receptor death domain and determination of its binding sites by NMR.

C. Analysis

1. Legal Standard

According to the M.P.E.P. § 2131, "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference".

Ilag *et al.* fail to teach an agent bound to a PTD domain.

Accordingly, Applicants submit that standard of strict identity to maintain a rejection under 35 U.S.C. § 102 has not been met. Withdrawal of the rejections under 35 U.S.C. § 102 is respectfully requested.

VIII Rejection under 35 C.F.R. § 103

Claims 21-23 and 25-30 were rejected under 35 U.S.C. §103 as allegedly obvious over Ilag *et al.*, Schwarze *et al.* (*Science*, 285:1569-1572, 1999), Voet *et al.* (Biochemistry, Second Edition, 1995, pp. 58-59), and Bertin *et al.* (U.S. Patent Application No. 2002/0061833).

These rejections are respectfully traversed.

A. The Present Invention is described above.

B. The Cited References

ILAG ET AL. is described above.

SCHWARZE ET AL. describe fusion proteins that contain an NH_2-terminal 11-amino acid protein transduction domain (PTD) for transduction of proteins.

VOET ET AL. list the amino acids and their residue mass.

BERTIN ET AL. relate to a method for determining whether a test compound alters the binding of CARD-3 to p75.

C. Analysis

According to the M.P.E.P. § 2143, "to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art references (or references when combined) must teach or suggest all the claim limitations."

The combination of Ilag *et al.*, Schwarze *et al.*, Voet *et al.*, and Bertin *et al.* fail to show or suggest the invention as a whole, including the nature of the results obtained. The combination of the presently claimed agents bound to a PDT domain attains superior advantageous effects over the disclosures of the cited references. Specifically, although Schwarze *et al.* teach fusion proteins containing an 11-amino acid PTD, this reference merely describes the introduction of the proteins into cells. One skilled in the art would have no way of knowing, absent a "try and see" approach, that the proteins will retrain their function. This is especially relevant to the agents of the present invention, which are involved in the signal transduction pathway acknowledged by the Examiner as complex. Nor do any of the other cited references make any mention of a PTD fusion protein.

Nor do the combined references teach a composition for regenerating nerves as presently claimed. Ilag *et al.* are limited to a discussion of the physiological role of Pep5 and make no mention of regenerating nerves. Schwarze *et al.* are not concerned with the biological function of the fusion proteins and make no mention of regenerating nerves. Voet *et al.* merely gives some physical data for the amino acids. Bertin *et al.* are concerned with proteins which bind to the intracellular domain of p75 to inhibit cell death.

In view of the above, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 103.

IX. Conclusion

In view of the foregoing, Applicants submit that the claims pending in the application are in condition for Allowance. A Notice of Allowance is therefore respectfully requested.

If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4410.

Respectfully submitted,
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Date: Feb. 14, 2006

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